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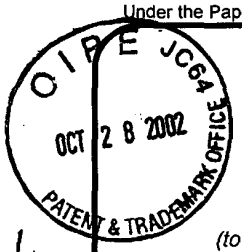


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# TRANSMITTAL FORM

*(to be used for all correspondence after initial filing)*

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|---|---|
| **Application Number** | 10/005,169 |
| **Filing Date** | December 4, 2001 |
| **First Named Inventor** | GUENTHER et al. |
| Group Art Unit | 1632 |
| Examiner Name | Bertoglio, V. |
| Total Number of Pages in This Submission | |
| Attorney Docket Number | R-687 |

## ENCLOSURES *(check all that apply)*

- [ ] Fee Transmittal Form
- [ ] Fee Attached
- [XX] ~~Amendment~~/ Reply to Restriction Requirement
- [ ] After Final
- [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
- [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Assignment Papers *(for an Application)*
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- [ ] Proprietary Information
- [ ] Status Letter
- [ ] Other Enclosure(s) *(please identify below)*:

Remarks



## SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

| | |
|---|---|
| Firm or Individual name | Kelly L. Quast, Reg. No. 52,141 DELTAGEN, INC. |
| Signature | Kelly L Quast |
| Date | October 18, 2002 |

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# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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|---|---|---|---|
| Applicant: | **Catherine GUENTHER et al.** | Group Art Unit: | **1632** |
| Serial No.: | **10/005,169** | Examiner: | **Bertoglio, Valerie** |
| Filed: | **December 4, 2001** | Customer No. | **26619** |
| Title: | **Transgenic Mice Containing NOR1 Gene Disruptions** | Docket/Order No. | **R-687** |
| | | Date: | **October 18, 2002** |

## RESPONSE TO RESTRICTION REQUIREMENT



Commissioner for Patents
Washington, D.C. 20231

Sir:

In response to the Office Action mailed September 19, 2002, concerning the Examiner's restriction to the claims, Applicants hereby provisionally elect, with traverse, Invention III (claims 8, 10, 14, 15, 18 and 19), drawn to a non-human transgenic animal and methods of making the animal.

In the restriction, the Examiner asserts that claims 1-26 are drawn to eight distinct subjects, grouped as: Invention I (claims 1-4), drawn to a gene targeting construct and a method of producing the gene targeting construct; Invention II (claims 5-7 and 9), drawn to a genetically modified animal cell; Invention III (claims 8, 10, 14, 15, 18 and 19), drawn to a non-human transgenic animal and methods of making the animal; Invention IV (claims 11, 13, 16, 17, 20, 21 and 23), drawn to methods of using a non-human, transgenic animal with a disruption in the NOR1 gene to screen for agents that modulate NOR1, and the agent so identified; Invention V (claims 12 and 13), drawn to a method of identifying an agent that modulates NOR1 by contacting the agent to a cell with a disruption in the NOR1 gene and the agent so identified; Invention VI (claims 22 and 23), drawn to an agent that inhibits NOR1, by contacting the agent to a cell that expresses the NOR1 gene, and the agent so identified; Invention VII (claims 24 and 25), drawn to a method of treating impaired balance or motor coordination; and Invention VIII (claim 26), drawn to a pharmaceutical composition containing NOR1. Applicants respectfully request reconsideration and withdrawal of the requirement.

Specifically, the Examiner asserts that the claims of Invention I and Invention II are patentably distinct in that the nucleic acid construct of Invention I can be used as a probe while the cells of Invention II can be used in *in vitro* assays of NOR1 function. The Applicants disagree with the Examiner's conclusion. Applicants believe that a reasonable search or examination of the prior art would produce results related to the subject matter of both invention groups, and would not put serious burden on the Examiner.

The Examiner also asserts that the claims of Invention I and Invention III are patentably distinct in that the construct of Invention I can be used to transfect cells *in vitro* while the mouse of Invention III can be used as a model of disease. The Applicants disagree with the Examiner's conclusion. Any search or examination of the prior art conducted on one of these aspects, *e.g.* production of NOR1 deficient transgenic animals, would produce results that would encompass the transgenic animals and the nucleic acid construct. Thus, the additional burden of a separate search or examination would not be required.

It is also asserted by the Examiner that the claims of Invention I and Inventions IV, V or VI are patentably distinct in that the nucleic acid construct of Invention I can be used as a probe while the methods of Inventions IV, V or VI can be used to identify agents that modulate (Inventions IV and V) or inhibit (Invention VI) NOR1. The Applicants disagree with the Examiner's conclusion. The Applicants believe that a reasonable search of the prior art would produce results related to NOR1 nucleic acid constructs and methods of identifying NOR1 modulators. A search and examination of the claims of each of these inventions, therefore, can be made without additional burden on the Examiner.

The Examiner also asserts that the claims of Invention I and Invention VII are patentably distinct in that the nucleic acid construct of Invention I can be used as a probe while the methods of Invention VII can be used to treat impaired balance or motor coordination. The Applicants disagree with the Examiner's assertion. A search or examination of the prior art conducted on the subject matter of Inventions I and VII would produce results encompassing NOR1 nucleic acid constructs and methods of using NOR1 to treat NOR1 related disorders such as impaired balance or motor coordination. Thus, a search or examination of these claims would not seriously burden the Examiner.

The Examiner further asserts that the claims of Inventions I-VI or VII and Invention VIII are patentably distinct in that the nucleic acid construct of Invention I, the cells of Invention II,

the transgenics of Invention III, the NOR1 modulators of Inventions IV-VI and the method of treatment of Invention VII are not necessary for the pharmaceutical composition of Invention VIII, and the pharmaceutical composition of Invention VIII is not needed for the compositions and methods recited in the claims of Inventions I-VII. The Applicants disagree with the Examiner's assertion, and believe a search and examination of the claims of Invention I-VI or VII and Invention VIII can be made without undue burden on the Examiner.

According to the Examiner, Invention II and Invention III are related as product and process of use, respectively. The Examiner asserts that Invention II and Invention III are patentably distinct because the transgenic animals and methods of making the animals of Invention III do not necessarily require the cells of Invention II and the cells can be used for distinctly different processes, such as screening compounds. The Applicants disagree with the Examiner's conclusion. Any search or examination of the prior art with regard to this subject matter, *i.e.,* NOR1 disruptions, would produce results encompassing both cells and animals with disruptions in NOR1. Thus, the burden of an additional separate search or examination would not be required.

The Examiner asserts that the claims of Invention II and Invention IV are patentably distinct because they can be used for different functions, and in particular, because the cells of Invention II can be used *in vitro* to determine the effects of a NOR1 disruption on gene expression while the methods of Invention IV can be used to identify agents that modulate NOR1 expression *in vivo.* The Applicants disagree with the Examiner's conclusion. Any search or examination of the prior art on one of these aspects, *e.g.* NOR1 disrupted cells, would produce results that would include the subject matter of both Inventions II and IV. Therefore, a search and examination of the claims of Inventions II and IV can be made without serious burden on the Examiner.

The Examiner further asserts that the claims of Invention II and Inventions V or VI are related as product and process of use, respectively. The Examiner states that the inventions are patentably distinct in that the agents that modulate NOR1 expression or activity recited in Invention V and Invention VI can be identified using transgenic animals or *in vitro* protein and DNA binding experiments, while the cells of Invention II can be used in differential expression assays. The Applicants disagree with the Examiner's assertion. A search or examination of the

prior art related to the subject matter of Invention II and Inventions V or VI would not place an undue burden on the Examiner.

The Examiner asserts that the claims of Invention II and Invention VII are patentably distinct because the cells of Invention II and the methods of Invention VII can be used for different purposes, namely to make a protein or test gene expression and to treat disease, respectively. The Applicants disagree with the Examiner's assertion. Any search or examination of the prior art on, *e.g.* NOR1 disruptions, would produce results that would include the subject matter of both Inventions II and VII. A search and examination of the claims of both Inventions II and VII, therefore, can be made without serious burden on the Examiner.

The Examiner asserts that the claims of Invention III and Invention IV are related as product and process of use. The Examiner states that the two inventions are patentably distinct as the agents recited in the claims of Invention IV can be identified by means other than the transgenic animals in Invention III, and the transgenic animals can be used for other purposes than identifying the agents, such as for phenotypic analysis. The Applicants disagree with the Examiner's assertion. A search of the prior art regarding the subject matter of both Inventions III and IV would reasonably produce results encompassing both the transgenic animal and methods of making the animal in Invention III as well as the methods of using the transgenic animal in Invention IV. Therefore, serious burden on the Examiner would not result from a search and examination of the claims of Inventions III and IV.

The Examiner further asserts that the claims of Invention III and Invention V or VI are patentably distinct in that the transgenic animals of Invention III can be used as an *in vivo* disease model, while the methods of Invention V and Invention VI can be used to identify an agent. The Applicants disagree with the Examiner's conclusion. Any search of the prior art related to, *e.g.* the transgenic animals of Invention III would include results related to NOR1 function, such as the methods of identifying NOR1 modulators recited in Inventions V or VI. A search and examination of the claims of Invention III and Inventions V and/or VI can be made without serious burden on the Examiner.

The Examiner further concludes that the claims of Invention III and Invention VII are patentably distinct in that the transgenic animals of Invention III can be used as an *in vivo* disease model while the methods of Invention VII can be used to treat disease. The Applicants disagree with the Examiner's conclusion. The Applicants do not believe that an undue burden

would be placed on the Examiner in order to search the prior art regarding the subject matter of both Inventions III and VII.

The Examiner also concludes that the claims of Inventions IV and Inventions V or VI are patentably distinct in that the methods of Invention IV are materially different from the methods of Inventions V and VI. Specifically, the Examiner suggests that the methods recited in the claims of Inventions IV make use of transgenic animals while Inventions V and VI use cells. The Applicants disagree with the Examiner's conclusion in that the methods recited in the claims of Inventions IV and the methods recited in the claims of Inventions V and VI use similar methods. A search of the prior art on the methods of Inventions IV and Inventions V or VI can be made without placing a serious burden on the Examiner.

The Examiner further concludes that the claims of Inventions IV, V or VI and Invention VII are patentably distinct in that the inventions can be used for different functions. Specifically, the methods recited in the claims of Inventions IV, V and VI can be used to identify modulators of NOR1, while the methods recited in the claims of Invention VII can be used to treat impaired balance or motor coordination. The Applicants disagree with the Examiner's conclusion. Any search or examination of the prior art related to the subject matter of Inventions IV, V or VI and Invention VII can be made without serious or undue burden on the Examiner.

Finally, with respect to the claims of Invention V and Invention VI, the Examiner concludes that the inventions are patentably distinct because each is directed to products that differ considerably in composition, structure and function. Specifically, the Examiner claims that Invention V is directed to modulators of NOR1 expression or activity while Invention VI is directed specifically to inhibitors of NOR1 activity. The Applicants disagree with the Examiner's conclusion. In particular, the Applicants respectfully point out that the Examiner has classified the claims of Invention V and Invention VI in the same class and subclass (class 530, subclass 350). Any search or examination of the prior art regarding these aspects, *i.e.* methods of identifying agents that modulate NOR1 using transgenic cells, would produce results that would encompass inhibitors and modulators of NOR1 and methods of identifying such agents. Thus, the additional burden of a separate search or examination would not be required in order to search the claims of both Inventions V and VI.

Although the Applicants have provisionally elected Invention III for the purposes of advancing prosecution of the present application, Applicants contend for the foregoing reasons

that the restriction requirement is improper. Accordingly, Applicants respectfully request reconsideration and withdrawal of the requirement.

Respectfully submitted,

Date: 10/18/02

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Name: **Deborah A. Mojarro**
Signed: _____ Date: 10-18-02